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HTLV-I SEROCONVERSION STUDY

ANNUAL/FINAL REPORT

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A study site was established on Okinawa, a hyperendemic area for the human T-cell leukemia virus-I (HTLV-I), for the purpose of studying the risk of HTLV-I transmission to the active duty personnel stationed there. Research activities completed include an HTLV-I seroprevalence survey and a prospective study for HTLV seroconversion. A cross-sectional HTLV serologic survey was conducted among 5,255 active duty U.S. Marines on permanent tour stationed in Okinawa, Japan to search for risk factors of seropositivity. Participants were primarily young, Caucasian males. Three (0.06%) were confirmed positive for HTLV by western blot (WB) analysis, showing reactivity for core and envelope. All 3 seropositive cases have a history of prolonged sexual contact with Okinawan women, and two of the three are married to infected Okinawan

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wives. Two gave a prior history for gonorrhea, while all 3 were negative for syphilis and hepatitis B. No other risk factors associated with HTLV-I seropositivity in the U.S. population were identified. A banked sample from one individual obtained 8 months after initial sexual relations with his HTLV-I seropositive Okinawan spouse and 20 months before being retested in the survey, showed a pattern suggesting seroconversion.

A prospective HTLV seroconversion study was conducted in which active duty Marines were screened for HTLV on arrival to Okinawa and approximately 1 year later at the end of their tour. Among 2,876 personnel enrolled, 2 were seropositive on baseline (0.069%). Follow-up was completed on 2,072 (72%), with non-compliance primarily due to early deployment (i.e. Desert Storm). There were no seroconversions to HTLV in the cohort. Questionnaire data collected at the time of the repeat draw indicate that casual sexual contact with Okinawans is common (23%), although marriage is not (< 1.2%). Sexually transmitted diseases were reported by approximately 5%; however, the majority of cases were urethritis, not genital-ulcerative disease. The reasons for the low risk of HTLV transmission demonstrated in these studies most likely include inefficiency of female-to-male heterosexual transmission as well as a low frequency of sexual contact of the Marines with HTLV seropositive women, as the HTLV seroprevalence of Okinawan women ages 20-35 is 1-4%.

Other studies initiated include: 1) a couples study of active duty and retirees married to Okinawans; 2) the establishment of a registry for HTLV-infected Navy blood donors for long-term follow-up, to include descriptive, clinical, immunologic, and epidemiologic information; and 3) the utilization of seropositive samples accumulated in these studies for collaborative work on rapid diagnostics of HTLV.

FOREWORD

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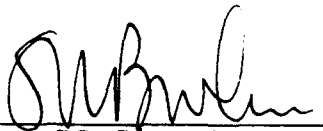

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TABLE OF CONTENTS

INTRODUCTION

Human T-Cell Leukemia/Lymphoma Virus Type I (HTLV-I), the first human retrovirus isolated, has been shown to be the etiologic agent for Adult T-Cell Leukemia/Lymphoma (ATLL) (1-4) and HTLV-I Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP) (5-8). The clinical syndrome of ATLL, distinguished by its aggressive clinical course and high frequency of skin involvement and hypercalcemia, was first described in the Southern Japanese island of Kyushu in 1977 (9). At that time, the clinical syndrome of ATLL was presumed to be secondary to an infectious agent due to the geographical clustering of the syndrome; however, the etiology was not known.

HTLV-I was first isolated at the National Cancer Institute from the peripheral lymphocytes and lymph node biopsy specimen of a patient who was presumed to have the T-cell leukemia, mycosis fungoides (1). Subsequently, Japanese researchers were able to demonstrate similar retroviral particles from the MT-1 cell line established from the peripheral blood of an ATL patient which they named the adult T-cell leukemia virus (ATLV). Using Indirect Immunofluorescence testing, antibodies to ATLV were detected in 44/44 ATL patients, and 32/40 patients with T-cell lymphoma with clinical characteristics similar to ATL (10). The etiologic link was further strengthened by demonstration of monoclonal integration of the HTLV-I provirus in the malignant cell. Isolates of HTLV-I from the United States and ATLV from Japan were later shown to have the same proviral sequences by Southern blotting techniques (11). HTLV-I is the current terminology for this Type C retrovirus.

Subsequent serosurveys documented HTLV-I seropositivity in patients with ATLL and further correlated endemic areas in Japan with the occurrence of ATLL. A north-south gradient of increasing HTLV-I seroprevalence was delineated, with population-based seroprevalence rates less than 1% in Northern Japan and as high as 37% in the ATL-endemic area of Nagasaki (2). Attention was drawn to the Caribbean when British investigators noted the similarities between the ATL cases reported by the Japanese and cases of 'T-lymphosarcoma-cell leukaemia' in blacks who had emigrated to Europe from the West Indies and Guyana (12). HTLV-I seropositivity was confirmed in these patients and in additional Caribbean population and hospital-based samples. Three communities in St. Vincent had a combined seroprevalence of 3.2% (3).

In 1985 it was reported that a disproportionate number of patients in the Caribbean basin with TSP were seropositive for HTLV-I (5). It is now known that HTLV-I is the etiologic agent in a subset of patients with this slowly progressive, primarily lower extremity myelopathy. Both ATLL and HAM/TSP

are characterized by a prolonged latent period between acquisition of infection and disease occurrence, with an estimated 'incubation' period of up to 4 or 5 decades. In addition, the risk of disease expression for both ATLL and HAM/TSP is low, with an estimated lifetime risk of disease of 1-4% (13).

Endemic areas which have been identified include the Ryukyu Island chain in Southern Japan, the Caribbean basin, parts of South and Central America, and Africa (Figure 1 in Appendices). These surveys have documented the focal pattern of seropositivity and disease occurrence now known to be characteristic of HTLV-I infection. Another unusual epidemiological feature of this virus is the rising seropositivity with age which occurs in all populations studied. Thus, the seroprevalence of infection can vary from 0 - 4% for individuals less than 20 years of age, to greater than 30% for individuals greater than 50 years of age. Three major mechanisms have been hypothesized to explain this: a cohort effect; perinatal infection with delayed seroconversion; and ongoing acquisition of infection during adulthood. There have been no data to support the existence of antibody-negative HTLV-I infection (14). The correlation with age is more likely related to ongoing infection during adulthood, perhaps combined with a cohort effect.

Most of the geographical areas of the world surveyed to date, including the United States, have low to negligible background seropositivity. Groups at higher than usual risk for HTLV-I infection in the United States population include blacks from endemic areas, intravenous drug users, recipients of multiple blood transfusions, female prostitutes, and, more recently, individuals with sexual contact with persons from endemic areas (13,15-17).

Transmission of HTLV-I occurs perinatally, sexually, and parenterally via blood transfusion or with intravenous drug abuse (13). Prospective studies have shown that approximately 15 - 20% of infants breast-fed by seropositive mothers will seroconvert versus 3% of infants who are bottle-fed. This suggests that the primary route of perinatal acquisition is via breast-feeding (18). Parenteral transmission via blood products requires cellular products (whole blood, packed cells, and/or platelets) with approximately 40 - 60% of the recipients seroconverting. Although studies of heterosexual transmission are limited, transmission appears to be relatively inefficient by this route, perhaps due to the highly cell-associated nature of the virus.

Okinawa has one of the highest endemic rates of HTLV-I in the world, with approximately 15%-40% of adults being infected (2,9,13). It is unique in the military as it is the only known hyperendemic region for HTLV-I where large numbers of troops and their dependents are being deployed for extended periods of time.

A cross-sectional HTLV seroprevalence survey was performed prior to the initiation of the prospective study in order to more rapidly approximate the seroprevalence of HTLV-I infection in active duty personnel on Okinawa, and to guide the design of the prospective study.

The objective of the 3-year prospective study was to define the risk of acquisition of HTLV-I in active duty troops stationed on Okinawa. This was felt to be particularly important at the time this study was initiated, as blood donors were not screened at the time for HTLV, and transmission of this virus to additional DOD personnel could have occurred through blood donation. Further, it was planned to identify risk behaviors and exposures associated with HTLV seropositivity. Active duty personnel were accessioned upon arrival to the island with a baseline HTLV serology. At the completion of a 1-year tour, a second HTLV serology was obtained to determine the rates of seroconversion.

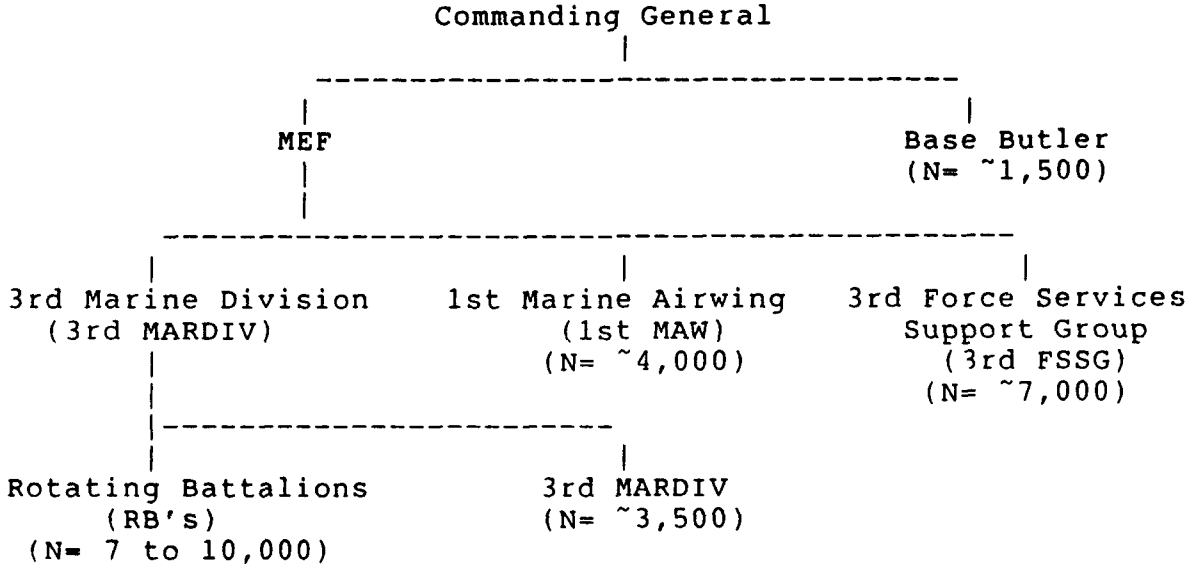
Additional activities which have resulted from this work have included: 1) initiation of a study of HTLV-I infection in retirees married to Okinawans; 2) initiation of a study of HTLV infection in Navy blood donors; 3) collaborative work with WRAIR and the CDC on diagnostics for HTLV; and 4) 4 published manuscripts, 4 meeting abstracts, and a chapter. These efforts are also described in this report.

I. SEROPREVALENCE SURVEY

Study Population:

Marine organization:

The Marine organization on Okinawa comes under the umbrella of the Marine Expeditionary Forces (MEF). Within the MEF, there are 3 primary components: Infantry (3rd Marine Division - 3rd MARDIV), Support (3rd Forces Service Support Group - 3rd FSSG), and Wing (1st Marine Airwing - 1st MAW). These 3 components are located on 6 bases on Okinawa (Figure 2 in Appendices). Base Butler is made up of non-deployable forces whose mission is to maintain the base support on Okinawa in the event of mass MEF deployment.



3rd MARDIV and 1st MAW have both permanent personnel and "rotators"--personnel who deploy to Okinawa for 6 months only. Actual time spent on Okinawa for these rotators may be as brief as 1 month or as long as 6 months, depending on the Pacific arena military exercises they participate in. The approximate strength of the 3rd MARDIV permanent personnel is 3,500 (vs. 7,000 to 10,000 in rotating battalions). 3rd FSSG (N= ~7,000) is made up primarily of "permanent" personnel serving either 1-year unaccompanied tours or 3-year accompanied tours. The approximate strength of the 1st MAW is 4,000 with the majority of these personnel being in rotating squadrons. The 1st MAW was excluded as the majority of personnel are rotators, the permanent personnel can be transferred between Okinawa and mainland Japan, and the mission of the Airwing is more easily disrupted by individual or unit research activities.

The study population was the permanent personnel in the 3rd MARDIV and 3rd FSSG (total N= ~10,000). Sera were collected over a 3-month period (April to July 1988) from active duty Marine Corps personnel of the 3rd MARDIV and 3rd FSSG. All Marine Corps personnel on Okinawa were required to have serologic testing for Human Immunodeficiency Virus (HIV) by October 1988. Permission was obtained by Navy medical personnel attached to the Marines to have the HTLV-I serologic survey done in conjunction with the mass HIV draws. Unit draws--organized primarily by company or battalion--were scheduled after completion of the Team Spirit Exercises in April and were continued until mid-July. Viral Epidemiology Project (VEP) staff were present for these draws to deliver a brief, administer a questionnaire and consent form, and draw blood. All personnel present were required to fill out a questionnaire; for those consenting, two consent forms (one copy for the individual to keep) were completed and 15 cc of blood was drawn.

Laboratory Methods:
Sera were frozen to -70°C and shipped in batches to Biotech Laboratories for inventory, with transfer to Program Resource Inc., Frederick Cancer Research Center, Fort Detrick, Maryland, and Biotech Laboratories, Rockville, Maryland for serology testing. All sera were screened with the Dupont/Biotech HTLV-I Enzyme Linked Immunosorbent Assay (ELISA), which utilizes whole disrupted virus as antigen. A cutoff ratio of 0.6 to positive control was considered positive. Additional initial screening included a p24-Radioimmune Assay (RIA) utilizing purified HTLV-I p24 as antigen. Samples were scored as positive if the counts were equal to or greater than 5% of the counts from a standard positive control. Confirmatory serologic screening included Western Blot (WB) to whole virus obtained from HUT-102 cells, which allows antibody detection against the principal antigens produced by HTLV-I core p19 and p24, and envelope gp46. Each WB was scored with an arbitrary scale: non-reactive (0), weak (0.5+), definite (1+), strong (2+), or very strong (3+). For a serum to be positive by WB, we required that antibodies of both the core (p19, p24) and envelope (gp46) gene products be present, regardless of the intensity or the presence of other bands. Sera without any WB reactivity (i.e., blank) were considered negative. All other WB profiles were labeled as indeterminate. A p21e WB, utilizing the envelope protein gp21e prepared via recombinant techniques, was also performed on all indeterminate or positive WB. Radioimmunoprecipitation Assay (RIPA), to enhance detection of antibody to the envelope glycoprotein (gp61/68) was used according to the method described by Essex (19) on sera with an indeterminate or positive WB pattern. Polymerase chain reaction (PCR) for HTLV-I/II was performed on peripheral blood mononuclear cells using the methods described by Ehrlich (20) in the WRAIR Retrovirology Laboratory and the University of Birmingham Retrovirology Laboratory.

Statistical Analysis:
Questionnaire data concerning demographics (e.g., rank, service occupation, base camp, time on Okinawa, marital status) and risk factors (e.g., other sexually transmitted diseases, drug abuse, prostitute contact, etc.) were computerized and verified by entering all data twice. All data were stored in a locked, secured area throughout the study to maintain confidentiality. Analyses were carried out separately for those who had been on the island 5 months or less versus those who had been on the island for more than 5 months. Frequencies were generated using the SPSSX program. Statistical tests and confidence intervals were utilized according to methods outlined by Fleiss (21).

Results:
Of the 7,001 active duty military personnel who had mandatory serologic screening for HIV over the study period, 6,707 individuals completed the questionnaire, and 78% (5,255/6,707) agreed to have HTLV-I testing done. The study population was predominately male (94.5%) (Table 1), with a mean age of 24.5 years and a racial distribution which included 67% Caucasians, 19% African Americans, 9% Hispanics, 2% Asian/Pacific Islanders, and approximately 3% other or not reported. While there were no significant differences between participants and non-participants for most demographic variables, participants had a higher level of education as compared to non-participants. Also, 30% of the non-participants were African Americans compared to 19% of the participants. Of the total participants, 1,323 (25.2%) had been on Okinawa for 5 months or less.

Twenty-eight of the 5,255 samples screened were positive by ELISA; one of these samples was also positive by p24 RIA. Of the 28 positive by ELISA, 3 were confirmed HTLV-I positive, having antibodies to both core and envelope proteins. Two of the three confirmed positives had diagnostic WBs, and the third had p19 and p24 bands on standard blot, p21e on enhanced WB, and gp 61/68 on RIPA. All 3 positive samples had p19 bands equal to or stronger than the p24 bands in intensity, which, according to the algorithm proposed by Wiktor, is consistent with HTLV-I (22). Sixteen were negative with no bands present. Nine had an indeterminate WB pattern, usually an isolated p24 or p19 band and a negative p21e enhanced WB. The overall HTLV-I seropositive rate for this sample was 0.06% (3/5,255). The rate for those residing in Okinawa for greater than 5 months was 0.076% (3/3,932), and no positive samples were noted in persons who had been on Okinawa less than 5 months.

The 3 seropositives were male: 2 Caucasian and 1 Korean/American (Table 2). None reported a history of blood transfusions, IV drug use, or sexual relations with an IV drug user, and none came from the Southeastern United States (24%

of the overall sample was from the Southeast). One of the three seropositives had two previous rotations in Okinawa. Two reported prior episodes of gonorrhea. All had a history of prolonged sexual relations with Okinawan women, with 2 being married to Okinawans. Both Okinawan wives were seropositive with antibodies to both core and envelope on WB, p21e band present, and gp 61/68 positive by RIPA. Physical exams were normal. Syphilis serology, including MHA-TP, and hepatitis B markers were negative.

Banked sera were available on one of the seropositive individuals (Case #1). This was 8 months after he had begun having sexual relations with his seropositive Okinawan wife, and 20 months before being detected as positive during the cross-sectional screen. This sample was ELISA positive, with p19 only on WB, RIA assay positive for gp61/68, and p21e WB positive. PCR was performed on cells from Case #3 and from his Okinawan wife, and both samples were positive for HTLV-I.

Conclusions:

Among 5,255 active duty United States Marines on permanent tour in Okinawa, Japan screened for HTLV-I seropositivity, 3 (0.06%) were confirmed by Western Blot analysis to have core and envelope reactivity. These findings suggest that the risk of transmission of HTLV-1 from the indigent population to active duty personnel stationed on Okinawa is low. However, a risk group of personnel with sexual contact to infected Okinawans was identified. All 3 seropositive cases have a history of prolonged sexual contact with Okinawan women, and two of the three patients are married to seropositive Okinawan wives. Two gave a prior history of gonorrhea, while all 3 were negative for syphilis (MHA-TP) and hepatitis B. No other risk factors associated with HTLV-I seropositivity in the United States were identified. These data, although based on small numbers, suggest a reservoir of exposure to HTLV-I via intimate contact with persons from HTLV-I viral endemic areas. Further, although based on small numbers, the negative syphilis serology suggests that female-to-male transmission of HTLV-I can occur in the absence of other cofactors, e.g., ulcerative genital lesions.

The efficiency of heterosexual transmission of HTLV-I is not well defined. However, it is thought to be transmitted relatively inefficiently, primarily because of the highly cell-associated nature of HTLV-I. Factors that appear to enhance transmission include the presence of genital ulcerative lesions, greater number of lifetime partners (in women), and an elevated HTLV-I antibody titer in the infected partner. Whether female-to-male transmission occurs sexually from husband to wife almost exclusively is a matter of controversy. The findings of a recent sexually transmitted diseases study in Jamaica correlated HTLV-I seropositivity with genital ulcerative disease (23). It was concluded that such cofactors may be required for female-to-male

transmission. The findings of our survey support the observation that heterosexual contact appears to be an inefficient mode of female-to-male transmission; however, it can occur even in the absence of previously identified cofactors. In this regard, the apparent seroconversion of one individual, detected 8 months following initial sexual contact with his seropositive spouse, lends support to this hypothesis.

Table 1: Demographic Characteristics of Participants and Non-Participants, HTLV-I Seroprevalence Study, Active Duty Marine Corps Personnel*, Okinawa, Japan, 1988

	Participants (N=5,255)			Non-Participants (N=1,452)		
	n	%	95% CI	n	%	95% CI
Sex:						
Male	4,966	94.50	93.84, 95.09	1,369	94.28	92.93, 95.40
Female	289	5.50	4.91, 6.16	93	5.72	4.60, 7.07
Age (mean):	5,255	(24.5)	24.3, 24.7	1,452	(24.9)	24.6, 25.2
Race:						
Caucasian	3,519	66.96	65.67, 68.23	802	55.23	52.63, 57.81
African American	1,021	19.43	18.37, 20.53	436	30.03	27.69, 32.47
Hispanic	488	9.29	8.52, 10.11	141	9.71	8.26, 11.38
Oriental	23	0.44	0.28, 0.67	10	0.69	0.35, 1.31
Pacific Islander	89	1.69	1.37, 2.09	26	1.79	1.20, 2.65
American Indian	71	1.35	1.06, 1.71	17	1.17	0.71, 1.91
Other/Not reported	44	0.84	0.62, 1.13	20	1.38	0.71, 1.91
Marital status:						
Single	3,107	59.12	57.78, 60.46	876	60.33	57.76, 62.85
Married	1,922	36.58	36.27, 37.90	522	35.95	33.49, 38.49
Divorced/Separated	222	4.22	3.70, 4.81	50	3.44	2.59, 4.55
Other/Not reported	4	0.08	0.02, 0.21	4	0.28	0.09, 0.76
Education:						
≤HS Graduate	4,655	88.60	87.63, 89.37	1,336	92.01	90.17, 93.08
College	600	11.40	10.58, 12.32	116	7.99	6.67, 9.53
Previous duty on Okinawa:						
Yes	1,007	19.16	18.11, 20.26	237	16.32	14.48, 18.35
No	4,246	80.80	79.70, 81.85	1,212	83.47	81.44, 85.33
Not reported	2	0.04	0.01, 0.15	3	0.21	0.05, 0.66

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

Table 2.
Characteristics of HTLV-I Seropositive Active Duty Marine Corps Personnel*, Okinawa, Japan, 1988

Case	Age	Sex	Race	Birth place	Time on Okinawa	Immunoblot bands positive	Risk factors
1	50	M	White	New York, New York	28 months	p19, p24, p21e	Okinawan spouse with HTLV-I infection; multiple Okinawan sexual partners
2	21	M	White	Boulder, Colorado	5 months	p19, p24, gp46, p21e	Okinawan sexual partner
3	27	M	Korean-American	Seoul, Korea	8 months	p19, p24, gp46, p21e	Japanese/Okinawan spouse with HTLV-I infection

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG, MEF

II. PROSPECTIVE HTLV-I SEROCONVERSION STUDY

Study Population:
The study population was permanent personnel assigned to 3rd MARDIV at Camp Courtney or 3rd FSSG at Camp Kinser. As all incoming active duty personnel must check in their medical records at the Battalion Aid Station (BAS) within one week of arrival, the BAS was chosen as the accessioning site. Commencing July 1988 and ending May 1990, all active duty personnel checking in to either of these BASs were directed to the VEP study staff by the BAS medical staff. Study enrollment was the same as described previously, with each individual filling out a questionnaire and consent form, and donating 15 cc of blood. A second sample and a follow-up questionnaire were obtained approximately 1 year later, prior to rotation off the island. Individuals identified as HTLV seropositive on baseline HTLV serology, or with repeat HTLV serology (seroconvertors), had a second sample drawn for confirmation. Confirmed HTLV seropositives had a full physical examination, were counseled by a study investigator, and a more detailed questionnaire was administered.

Laboratory Methods:
The laboratory methods were identical to those described previously (page 9).

Statistical Analysis:
Questionnaire data concerning demographics (e.g., rank, service occupation, base camp, time on Okinawa, marital status) and risk factors (e.g., other sexually transmitted diseases, drug abuse, prostitute contact, etc.) were computerized and verified by entering all data twice. The data were stored in a locked, secured area throughout the study to maintain confidentiality. Frequencies were generated using the SPSSX program. Statistical tests and confidence intervals were calculated according to methods outlined by Fleiss (21).

Results:
Demographic characteristics:
Enrollment of 2,876 subjects for the prospective study was completed in June 1990. A total of 2,052 subjects from Camp Kinser (FSSG) and 824 subjects from Camp Courtney (Marine Division) were enrolled. There were no significant differences between the demographic composition of enrolled personnel from Camp Courtney and Camp Kinser; therefore the descriptive data from these two cohorts were combined. A comparative analysis between participant and non-participant demographic information at enrollment revealed a slight

difference between the proportion of caucasians and African Americans participating. There was a slightly higher proportion of African Americans not participating than those participating and more caucasians participated than did not participate. In addition, a significant difference existed between personnel who have had a previous duty assignment on Okinawa. A larger proportion of individuals who have had previous duty assignments on Okinawa did not participate in the study, however this question was not recorded for more than half of those not participating because this quesion was added to the questionnaire after it had been implemented. Table 3 displays the deomographic values between these populations at enrollment. The enrolled sample was predominantly male, with a mean age of 24 years and a racial distribution of 64% Caucasians, 22% African Americans, 10% Hispanics, 2% Asian/Pacific Islanders, and 2% other. The majority of participants were single, with 36% being married and 4% divorced or separated. Eighty-nine percent had up to a high school education, with approximately 11% having an associates or more advanced degree.

HTLV seroprevalence:
The overall baseline HTLV-I seropositivity rate was 0.07% (2/2,876). Thirty-eight subjects had a repeatedly reactive screening ELISA, with 36 being negative by Western Blot (WB). One subject was confirmed positive on WB and by Radioimmunoprecipitation Assay (RIPA), with polymerase chain reaction (PCR) confirming HTLV-I. This individual is a black male from Trinidad, an endemic area for HTLV-I. He is asymptomatic with a normal physical examination, normal peripheral blood smear, and negative VDRL. His long-term female partner screened negative for HTLV. The second individual had a serologic pattern more consistent with HTLV-II (p24 > p19, p21e present, without gp48 or gp61/68 on RIPA), and PCR has confirmed HTLV-II infection.

A follow-up blood draw has been done on 2,072 subjects with a mean duration of follow-up of 344 days and a total of 1,953 person-years of observation. The follow-up process was hindered by the rapid, massive deployments in Operation Desert Shield/Storm. The overall compliance rate is estimated to be 72%. Sixteen subjects refused to provide a second blood specimen, and 788 individuals were lost to follow-up due to early rotation, deployment, or non-compliance with the request for a return visit. A comparative analysis between those tested and those who did not complete the testing process revealed no significant differences in age, race, sex, marital status, educational background, nor paygrade. Table 4 displays the demographic information on these groups.

Table 3: Demographic Characteristics of Participants and Non-Participants, Prospective HTLV-I Seroconversion Study, Active Duty Marine Corps Personnel, Okinawa, Japan, 1988-1990

	Participants (N=2,876)			Non-Participants (N=932)		
	n	%	95% CI	n	%	95% CI
Sex: Male	2,564	89.1	87.9, 90.3	813	87.2	84.9, 89.3
Female	312	10.9	9.7, 12.0	119	12.8	10.7, 15.1
Age (mean):	2,876	(23.96)	22.4, 25.6	932	(24.33)	21.6, 27.1
Race:						
Caucasian	1,841	64.0	62.2, 65.8	507	54.3	51.1, 57.6
African American	634	22.1	20.5, 23.6	312	33.5	30.4, 36.6
Hispanic	293	10.2	9.1, 11.4	83	8.9	7.1, 10.9
Asian (Chinese/Jpnese)	16	0.6	0.3, 0.9	2	0.2	0.0, 0.8
SE Asian/Vietnamese	7	0.2	0.1, 0.5	4	0.4	0.1, 1.1
Pacific Islander/Phil.	35	1.2	0.8, 1.7	8	0.9	0.3, 1.7
American Indian	33	1.1	0.7, 1.6	7	0.8	0.3, 1.6
Other	17	0.6	0.3, 0.9	9	1.0	0.4, 1.8
Marital status:						
Single	1,709	59.4	57.6, 61.2	519	55.9	52.6, 59.1
Married	1,043	36.3	34.5, 38.1	370	39.8	36.6, 43.1
Divorced/Separated	123	4.3	3.5, 5.1	40	4.3	3.0, 5.8
Not reported	1	-	- -	3	-	- -
Education:						
≤HS Graduate	2,568	89.3	88.1, 90.4	826	89.1	86.8, 90.9
≥College	307	10.7	9.5, 11.9	102	10.9	9.0, 13.2
Not reported	1	-	- -	4	-	- -
Previous duty on Okinawa:						
Yes	507	17.6	16.2, 19.1	178	41.3	36.6, 46.1
No	2,367	82.4	80.9, 83.7	253	58.7	53.8, 63.4
Not reported	2	-	- -	501	-	- -

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

Table 4: Demographic Characteristics of Participants Tested and Not Tested, Prospective HTLV-I Seroconversion Study, Active Duty Marine Corps Personnel, Okinawa, Japan, 1988-1990

	Participants tested (N=2,072)			Not tested (N=804)		
	n	%	95% CI	n	%	95% CI
Sex: Male	1,858	89.7	88.2, 90.9	706	87.8	85.3, 90.0
Female	214	10.3	9.0, 11.7	98	12.2	10.0, 14.7
Age (mean):	2,072	(23.93)	22.1, 25.8	804	(24.05)	21.2, 27.1
Race:						
Caucasian	1,333	64.3	62.2, 66.4	508	63.2	59.7, 66.5
African American	452	21.8	20.0, 23.7	182	22.7	19.8, 25.7
Hispanic	203	9.8	8.5, 11.2	90	11.2	9.0, 13.6
Asian (Chinese/Jpnese)	11	0.5	0.2, 0.9	5	0.6	0.2, 1.4
SE Asian/Vietnamese	6	0.3	0.1, 0.6	1	0.1	0.0, 0.7
Pacific Islander/Phil.	30	1.5	0.9, 2.1	5	0.6	0.2, 1.4
American Indian	23	1.1	0.7, 1.7	10	1.2	0.5, 2.3
Other	14	0.7	0.3, 1.1	3	0.4	0.1, 1.1
Marital status:						
Single	1,250	60.3	58.1, 62.4	459	57.1	53.5, 60.5
Married	729	35.2	33.1, 37.3	314	39.1	35.6, 42.5
Divorced/Separated	92	4.5	3.5, 5.4	31	3.8	2.6, 5.4
Not reported	1	-	- -	0	-	- -
Education:						
≤HS Graduate	1,840	88.8	87.3, 90.1	728	90.5	88.3, 92.5
≥College	231	11.2	9.8, 12.6	76	9.5	7.5, 11.7
Not reported	1	-	- -	0	-	- -
Previous duty on Okinawa:						
Yes	350	16.9	15.3, 18.6	157	19.5	16.8, 22.4
No	1,721	83.1	81.3, 84.7	646	80.4	77.4, 83.0
Not reported	1	-	- -	1	0.1	- -

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

The 2 individuals identified as HTLV seropositive on the baseline serology were reconfirmed to be seropositive. Twenty-four subjects had a repeat reactive ELISA on follow-up serology; however, none of these were shown to be HTLV seroconvertors by WB. A summary of the more pertinent follow-up questionnaire data is located in the text (Table 5), and the remaining questionnaire data are included in the Appendices (Table A).

One-hundred-thirteen of the 2,072 subjects (5.5%) reported a sexually transmitted disease (STD) in the preceding year. Nongonococcal urethritis (NGU) was the most common STD reported (57%), with gonorrhea (21%) and genital warts (15%) being less common. Forty-five percent claimed the STD was contracted while on Okinawa, as compared to 15% in the Philippines and 9% in Korea. Six percent claimed the STD was contracted in the United States, and 25% did not identify an area where the STD was contracted. One hundred five individuals reported a history of dysuria during the preceding year, a possible surrogate for STDs. Of these, 48 did not report any STD.

Sexual contact with Okinawans during the preceding year was reported by approximately 23% of the population. The mean number of Okinawan sex partners was 2.6, and the median number of sexual encounters was six. One individual reported 365 sexual encounters; however, he is married to an Okinawan woman. The survey was modified after the study was initiated, based on results of the seroprevalence survey, to include a question on marriage to Okinawans. Marriage to Okinawans was found in 13 of 1,107 Marines (1.2%). Five of the 13 spouses have been ELISA tested to date and all were seronegative. The other spouses refused testing (n=6) or were not available (n=2).

Hepatitis A, B, and C testing is being performed on paired sera of the first 1,014 subjects. Prior hepatitis B infection was evident in 14/1,014 (1.4%) with a positive baseline hepatitis B core antibody, 3 subjects were also Hbsag positive (0.3%). Testing on the repeat sample is in progress, however the preliminary data shows at least two subjects seroconverted to hepatitis B (0.2%), with one of the two reporting acute hepatitis during the observation period. Seven subjects (0.7%) were positive for hepatitis C on ELISA, but only 2 (0.2%) had a confirmatory test, and there were no seroconversions to hepatitis C. Hepatitis A results are pending.

Table 5.
Self-Reported Sexually Transmitted Diseases
and Other Potential Risk Factors,
Prospective HTLV-I Seroconversion Study,
Active Duty Marine Corps Personnel*
Okinawa, Japan, 1989-1991

	Category	Number	Percent
STD:	Yes	113	5.5
	No	1,952	94.5
	Not reported	7	-
First STD type:	Syphilis	0	0.0
	Gonorrhea	24	21.2
	Non-gonococcal ureth.	64	56.7
	Genital warts	17	15.0
	Genital herpes	2	1.8
	Other	5	4.4
	Not reported	1	0.9
	Not applicable	1,959	-
Second STD type:	Gonorrhea	1	12.5
	Non-gonococcal ureth.	3	37.5
	Genital warts	1	12.5
	Other	1	12.5
	Not reported	2	25.0
	Not applicable	2,064	-
Location of STD contact:	United States	7	6.2
	Philippines	17	15.0
	Korea	10	8.9
	Okinawa	51	45.1
	Not reported	28	24.8
	Not applicable	1,959	-
Dysuria:	Yes	105	5.1
	No	1,957	94.9
	Unknown	10	-
Total:		**2,072**	

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

Table 5. continued
Self-Reported Sexually Transmitted Diseases
and Other Potential Risk Factors,
Prospective HTLV-I Seroconversion Study,
Active Duty Marine Corps Personnel*
Okinawa, Japan, 1988-1989

	Category	Number	Percent
Sex with Okinawans:	Yes	468	22.7
	No	1,591	77.3
	Unknown	13	-
Number of Okinawan sex partners:	Range	1 - 37	
	Median	1	
	Mean	2.6	
	Not reported	68	
	Not applicable	1,589	
Number of sexual encounters:	Range	1 - 365	
	Median	6	
	Mean	19.9	
	Not reported	106	
	Not applicable	1,589	
Okinawan spouse:	Yes	13	1.2
	No	1,094	98.8
	Unknown	965	-
Blood transfusion:	Yes	1	0.1
	No	1,808	99.9
	Unknown	263	-
Work with blood:	Yes	34	1.9
	No	1,755	98.1
	Unknown	283	-
Total:		2,072	

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

Conclusions:
Prospective 1-year follow-up of a large cohort of Marines with paired HTLV serologies did not demonstrate acquisition of HTLV infection despite prolonged deployment in an HTLV hyperendemic area. These findings corroborate the cross-sectional seroprevalence survey (pp. 6-12) in which HTLV was shown to be an infrequent infection (0.06%) in this population. Two individuals were HTLV seropositive on baseline screening. The individual confirmed to be HTLV-I infected was from Trinidad, an endemic area. The individual with HTLV-II infection denied known risk factors for HTLV-II (intravenous drug abuse (IVDA), transfusion recipient, or sexual partner with these risk factors). As a Puerto Rican from the Bronx in New York, he is in a high risk group for IVDA or intimate contact with IVDAs.

In the cross-sectional seroprevalence survey, the only risk factor identified in all three HTLV-I infected active duty cases was prolonged sexual contact with an Okinawan. One other individual on Okinawa who was not in the cross-sectional or cohort study was identified as HTLV-infected by the blood donor screening program during the period of this study. His only risk factor for HTLV-I infection was marriage to an HTLV-I infected Okinawan wife.

The reasons for the low risk of HTLV transmission demonstrated in these studies most likely include the inefficiency of female-to-male heterosexual transmission of this highly cell-associated virus. Sexual contact with the local Okinawan women was common among the prospective cohort, being reported by 23% of the Marines. Although the average seroprevalence of HTLV in the adult Okinawan population is 15-40%, the prevalence rises with age and is reported to be 1-4% in women aged 20 to 35 years. The results of the HTLV prenatal screening program in the Naval Hospital on Okinawa reveal a seroprevalence of approximately 4% (5/115) in Okinawan pregnant dependent wives.

The relative inefficiency of female-to-male transmission of HTLV-I was recently demonstrated in a prospective study of discordant couples followed in Miyazaki, Japan (24). There were 5 seroconversions in the 81 discordant couples over the 3-year period of follow-up. Four of 28 wives (14.3%) at risk seroconverted versus 1 of 53 husbands (1.9%). There was an association demonstrated between the presence of anti-Tax antibody and sexual transmission. It was theorized that as the Tax protein is known to promote transcriptional transactivation of the virus and cellular genes, the presence of anti-Tax protein may correlate with viral load. No interview data were available on these couples to evaluate the

presence of other possible risk factors.

Cofactors which are thought to enhance HTLV transmission include a history of genital ulcers, including syphilis. This most likely occurs through altering the mucosal barriers, and perhaps through an increased number locally of white cells, the host cell for HTLV. Although 5.5% of the population reported a STD during the period of follow-up, nongonococcal urethritis and gonorrhea were the most common, with no cases of syphilis and only 2 cases of genital herpes reported. In addition, the prostitutes on Okinawa are primarily imported in from other geographic areas, including Korea and the Philippines. Sexual contact with the local Okinawan women is thought to be mainly in the context of 'dating', further reducing the risk of coexisting STDs.

The finding of at least 2 seroconversions to hepatitis B in the 1014 (0.2%) personnel being tested for this is also of interest. This is 2-fold higher than a recent viral hepatitis incidence study of active duty Navy personnel assigned to two U.S. Navy ships (25). One of the two seroconverters reported acute clinical hepatitis. Both individuals had deployed to Korea during Team Spirit. A more in-depth investigation will be conducted once all of the cases have been identified. however Neither of these individuals worked in the medical/dental professions, and intravenous drug abuse appears to be uncommon in Okinawa. Thus it is most likely that these infections were sexually acquired. Although the comparative risks of exposure of active duty personnel to HTLV and hepatitis B are unknown, these data suggest that hepatitis B is more efficiently sexually transmitted.

III. COUPLES STUDY

Background:
The results of the seroprevalence survey and the prospective HTLV seroconversion study suggest that female-to-male heterosexual transmission is an uncommon event in the population studied, apparently requiring prolonged sexual contact. Further information regarding the correlates of heterosexual transmission would be useful, as this could provide a basis for recommendations in the counselling procedures for HTLV-I infected persons. This is now being done in conjunction with the mandatory screening of all blood donors.

There is a large population of U.S. military retirees residing on-island, most of whom are married to Okinawan women. Although there is no precise information as to the size of the population, it is estimated to be approximately 1,000-2,000. The seropositivity rates of HTLV-I increase with age in endemic populations, and the seropositive rates in Okinawan women over the age of 50 have been documented to be approximately 25-30%. As the retiree husbands are from a nonendemic area, this virtually eliminates the possibility for vertical transmission of HTLV-I, a factor which has confounded other family studies done in endemic areas. Thus, the retiree population on Okinawa provides a unique opportunity for study of female-to-male transmission of HTLV-I.

Study Population:
Retirees (married, single, or widowed) living on Okinawa are the target population. Retirees are being accessioned through a number of mechanisms including: 1) a flyer sent out from the American consulate's office; 2) presentations made to retiree organizations; and 3) through the primary care clinics in the Naval Hospital. Active duty personnel married to Okinawans are also eligible for the study and are being accessioned primarily through the Prenatal Clinic in the prenatal HTLV screening program. Informed consent written in English and Japanese will be obtained. A brief questionnaire asking only demographic information will be administered at the time of informed consent.

Laboratory Methods:
15 cc of blood will be collected from the retirees and their spouses to yield approximately 8 cc of sera. All sera will be screened with Abbott HTLV-I Enzyme Linked Immunosorbent Assay

(ELISA), which utilizes whole disrupted virus as antigen. A cutoff ratio of 0.6 to positive control is considered positive. Confirmatory serologic screening includes Western Blot (WB) to whole virus obtained from HUT-102 cells, which allows antibody detection against the principal antigens produced by HTLV-I core p19 and p24, and envelope gp46. Each WB is scored with an arbitrary scale: non-reactive (0), weak (0.5+), definite (1+), strong (2+), or very strong (3+). For a serum to be positive by WB, antibodies of both the core (p19, p24) and envelope (gp46) gene products must be present, regardless of the presence or intensity of other bands. Sera without any WB reactivity (i.e., blank) are considered negative. All other WB profiles are labeled as indeterminate. A p21e WB, utilizing the envelope protein gp21e prepared via recombinant techniques, is also performed on all indeterminate or positive WBs. Radioimmunoprecipitation Assay (RIPA), to enhance detection of antibody to the envelope glycoprotein (gp61/68), is used according to the method described by Essex (19) on sera with an indeterminate or positive WB pattern. Individuals confirmed seropositive will have 15 cc of blood collected for cell analysis with polymerase chain reaction (PCR). PCR for HTLV-I/II is performed on peripheral blood mononuclear cells using the methods described by Ehrlich et al. (20) in the WRAIR Retrovirology Laboratory.

Statistical Analysis:
Questionnaire data will be analyzed for demographic and risk factors described in the questionnaire. A follow-up questionnaire with more detailed information will be administered to subjects identified as HTLV seropositive and their spouses. A random numbers table will be utilized to select 4 seronegative spouse pair controls for each couple with either or both spouses seropositive. All data will be stored in the project location on Okinawa in a locked filing cabinet in a secured area to maintain confidentiality. Copies will be mailed to the Naval Health Research Center (NHRC) for data entry. Data will be entered to the NHRC VAX computer with analyses using SPSSX and BMDP software.

Preliminary Results:
To date, 59 retirees, 7 active duty members, and 26 spouses have been enrolled. The mean age of the retirees was 59 years with a range of 38 - 78 years, and eighty-five percent were caucasian. The majority of the retirees were married (n=43), with the remaining individuals being single (n=3), divorced (n=1), widowed (n=3), or of unknown marital status (n=9) (Table 6). The mean duration of their relationships was 24.5 years with a range of 4 - 40 years. Of the retiree spouses,

one was male, 17 of 19 were Okinawan, with a mean age of 48 years and a range of 29 - 63. To date, all of the retirees and their Okinawan spouses (n=17) have been seronegative for HTLV. The mean age of the seven active duty personnel was 32 years with a range of 21 - 50 years, and all were caucasian. Six were married and one was single. The mean duration of their relationships was 10.7 years. All of the active duty spouses were from Okinawa, they had a mean age of 36 and a range of 25 to 52 years. One of the 52 year old Okinawan spouses was HTLV-I infected as was her 50 year old active duty Air Force husband. Of note, this couple has been married for approximately 25 years and was accessioned through the Internal Medicine Clinic where the Okinawan wife had presented with chronic sinusitis. On further evaluation she was diagnosed with chronic ATL. To date, this study has found an overall seroprevalence of HTLV-I infections in the Okinawan spouses to be 4.2% (1/24).

Conclusions:

The reasons for the apparently lower seroprevalence of HTLV in the Okinawan spouses married to active duty and retiree personnel versus the seroprevalence documented in the general population are not entirely clear. An average seroprevalence rate of 15% with rates >30% in women older than 50 have been reported in the literature and verified as accurate by colleagues at Chubu, the local Prefecture hospital. As our study is in the preliminary stages, the small sample size and/or selection bias may account for this low rate. Another possibility is that the seropositivity rates in the Okinawan population previously published and currently reported by the Chubu staff for the Okinawan population are falsely elevated due to utilization of less specific serologic techniques, such as latex agglutination. To address this possibility, sera previously collected and tested by a competitive binding assay from patients at Chubu Hospital, Okinawa in 1985 (9) was retested with the current technology which has increased specificity. The results, as shown at the top of the next page, revealed similar outcomes, particularly if p21e, a more sensitive assay for envelope protein, can be substituted for gp46 on the WB (modified criteria).

Association	Testing Criteria: Clark, et al. (9)	Current technology Strict	Modified
Adult T-cell leukemia-lymphoma	7/7	7/7	7/7
Non-Hodgkin's lymphoma	2/5	2/5	2/5
Hematological diseases	3/8	3/8	3/8
Strongyloides	2/2	2/2	2/2
Dermatological diseases	1/1	1/1	1/1
Lymphadenopathy	1/1	1/1	1/1
Family members with ATL	3/4	2/4	3/4
Other asymptomatic diagnoses	19/129	10/129	15/129

When the asymptomatic group was analyzed according to age, the following differences were found:

Age	Clark, et al. (9)	Strict	Modified
<50 years	3/77 (4%)	1/77 (1%)	3/77 (4%)
≥50 years	16/52 (30%)	9/52 (17%)	12/52 (23%)

There is mounting evidence to support heterosexual transmission as the major explanation for the rising incidence of HTLV-I seroprevalence with increasing age, which is the typical pattern in endemic populations. Thus, a final and perhaps more probable explanation is that Okinawan women married to men from a non-endemic region are at low risk of acquiring HTLV-I infection from their spouse. If this was the case, one would expect HTLV-I seroprevalence rates to approximate the rates documented at the age of marriage to American personnel. Data collected from the ongoing prenatal HTLV screening program at Naval Hospital Okinawa supports this theory. The seropositivity rate of HTLV-I in these younger women is 4% (4/98), which is the same rate that is observed in the preliminary data of the couples study.

Table 6.
Demographic Characteristics of Participants in the HTLV-I Couples Study, Active Duty and Retired [Navy and] Marine Corps Personnel and Spouses, Okinawa, Japan, 1991-1992

Active Duty:	N = 7		
Age in years:	Mean:	31.8	
	Range:	21 - 50	
Sex:	Male	7	
	Female	0	
Race:	White	7	
Education:	High school grad/GED	5	
	Bachelor's degree	2	
Marital status:	Single	1	
	Married	6	
Number of children:	None	2	
	Two	1	
	Not reported	4	
Duration of relationship in years:	Mean:	10.7	
	Median:	12	
	Range:	1 - 25	

Table 6. continued
Demographic Characteristics of Participants in the
HTLV-I Couples Study, Active Duty and Retired [Navy and]
Marine Corps Personnel and Spouses, Okinawa, Japan, 1991-1992

Retiree:	N = 59				
Age in years:	Mean:	59.2	Range:	38 - 78	
Sex:	Male	58	Female	1	
Race:	White	50	American Indian	1	
	African American	4	Japanese	2	
	Hispanic	1	Other	1	
Education:	Some high school	4	Associate degree	2	
	High school grad/GED	18	Bachelor's degree	7	
	Some college	13	Master's or higher	4	
	Not reported	10			
Marital status:	Single	3	Divorced/separ.	1	
	Married	43	Widowed	3	
	Not reported	9			
Number of children:	None	21	Three	2	
	One	12	Four	2	
	Two	8	Not reported	13	
Duration of relationship in years:					
	Mean:	24.5	Median:	22	
	Range:	4 - 40	Not reported:	13	

Spouse of active duty or retiree:	N = 26			
Age in years:	Mean:	45.0	Range:	25 - 63
Sex:	Male	1		
	Female	25		
Race:	Okinawan	24		
	Japanese (not from Okinawa)	1		
	Chinese	1		

IV. BLOOD DONOR STUDY

As of March 1989, all blood donors were screened for HTLV-I/II infection. The Navy has 17 blood donor centers at Medical Treatment Facilities in Conus, and 7 donor centers overseas. Sera that are repeatedly reactive by HTLV ELISA are sent to the WRAIR Retrovirology Laboratory for confirmatory testing. A preliminary analysis of the Navy Blood Donor HTLV screening program was performed. From March 1989 to June 1990, 62,271 Navy blood donors were screened for HTLV-I/II. Twenty-five sera were repeat reactive by ELISA, and 10 confirmed positive. An additional 5 donors were referred from civilian or Army donor centers. Of the 15 seropositive donors, polymerase chain reaction (PCR) for HTLV-I/II differentiation was available on 12. Eight of the seropositives were confirmed to be HTLV-I, and 4 were HTLV-II. PCR results were unavailable on 3 individuals due to inaccessibility (n=2) or refusal for a repeat blood draw (n=1). Six of the spouses were tested, and 4 were HTLV seropositive.

Risk factor information is available on 11 of the 12 individuals. Four of the six individuals with HTLV-I infection were from an endemic area (Panama, Santiago, Chile, Trinidad, Dominican Republic). The other two individuals are active duty Marines married to seropositive Okinawans. HTLV-II infection was associated with different risk factors: blood transfusion (n=1), history of intravenous drug abuse (IVDA) (n=1), marriage to an IVDA (n=1), and American Indian origin (n=1). These results show that HTLV is an infrequent infection in the Navy blood donor population (0.016%). The finding of coinfection in 4 of the 6 spouses tested underlines the need to include testing of the spouse in the counseling procedures. Finally, as both HTLV-I and HTLV-II are present in DOD seropositive donors, procedures to distinguish which virus is present in seropositive individuals must be performed for appropriate counseling.

V. RAPID DIAGNOSTICS

Diagnosis of HTLV I/II remains problematic. The criteria most often used for determining HTLV seropositivity requires the demonstration of antibodies against the gag (p24) and env (gp46 or gp68) gene products (26). Unlike HIV, the western blot is usually nondiagnostic, particularly in the U.S. population. Confirmation then requires radioimmune precipitation assay (RIPA), which is costly, labor intensive, and not widely available. An additional problem is distinguishing between HTLV-I and HTLV-II. While most of the serologic assays were originally designed to detect HTLV-I, they also detect antibodies to HTLV-II, due to significant homology of structural proteins between HTLV-I and HTLV-II (27). Currently, the most reliable technique used to differentiate between HTLV infections is by genetic amplication using polymerase chain reaction (PCR) analysis (28). However, PCR requiring lymphocytes isolated from the donor is technically complex and therefore not well suited for the routine clinical laboratory. There is a need for HTLV rapid diagnostic serologic tests for blood donor screening, patient evaluation, and for epidemiolgic surveys. Serologic tests for confirmation and differentiation of HTLV infection are being developed. Analysis of the performance of these assays requires a diverse array of samples, such as can be provided through the DOD blood donor screening program and through study sites established in hyperendemic areas, such as Okinawa. A collaborative effort has been established with the CDC, the WRAIR Retrovirology laboratory, and the HTLV Project to systematically evaluate these new technologies.

Collaborative efforts have primarily been in the area of differentiation of HTLV-I from HTLV-II: via application of an algorithm, use of recombinant envelope protein on WB, and by synthetic peptide immunoassays. Of the three types of methodologies studied, the algorithm using the relative intensities of the p24 and p19 bands was the least specific with 92% specificity. The addition of the rgp21 recombinant envelope to the whole virus WB improved the sensitivity and specifity; however, false positives occurred particularly in the setting of an indeterminate pattern (gag protein only on WB and RIPA). Most promising has been the use of the synthetic peptide immunoassays, SynthEIA and Select-HTLV, which did not misclassify any specimens. Sensitivity was higher with the Select-HTLV (98% HTLV-I, 95% HTLV-II) vs the Synth-EIA (95% HTLV-I, 76% HTLV-II). (see Manuscripts section for references).

SUMMARY

In summary, the results of the cross-sectional HTLV-I seroprevalence and the prospective HTLV seroconversion studies in U.S. Marines on Okinawa show that transmission of this virus from the indigent population to active duty personnel is negligible. Active duty personnel with prolonged sexual relations with seropositive Okinawan women have been identified as a risk group for acquisition of infection. The efficiency of heterosexual transmission is not well defined. A more exact determination of the correlates of female to male transmission would be useful as it could provide a basis for recommendations for prevention. There is preliminary data that products of tax, a nonstructural, regulatory gene, may play a role in transmissibility of HTLV with the presence of antibody to tax having an apparent positive correlation with seroconversion (24). This observation needs to be confirmed in other populations of discordant and concordant spouse pairs such as can be found in the couples study and the blood donor study. Additionally other markers or risk factors for transmission need to be defined.

The clinical outcomes of HTLV-I infection, ATLL and HAM/TSP, both have a prolonged latency period of up to several decades for disease expression. This emphasizes the importance of long-term follow-up of a seropositive cohort in order to delineate the full spectrum of disease outcomes. DOD health care beneficiaries, identified through blood donor and clinical screening, are an ideal population in which to establish such a cohort.

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APPENDICES

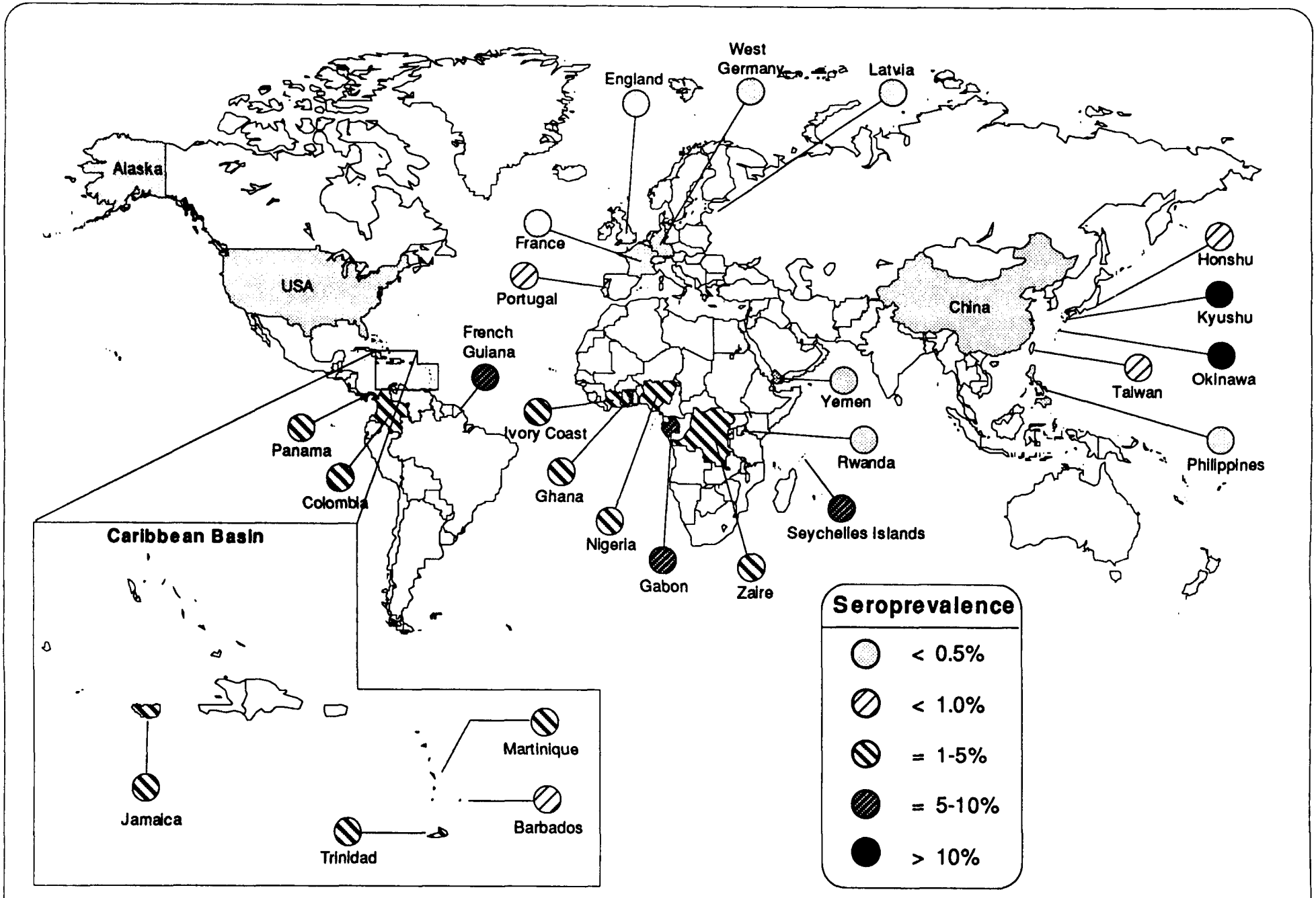

FIGURE 1. World map showing representative HTLV-I seroprevalence studies. Various types of population studies are displayed including blood donors, clinical patients, and general population studies.

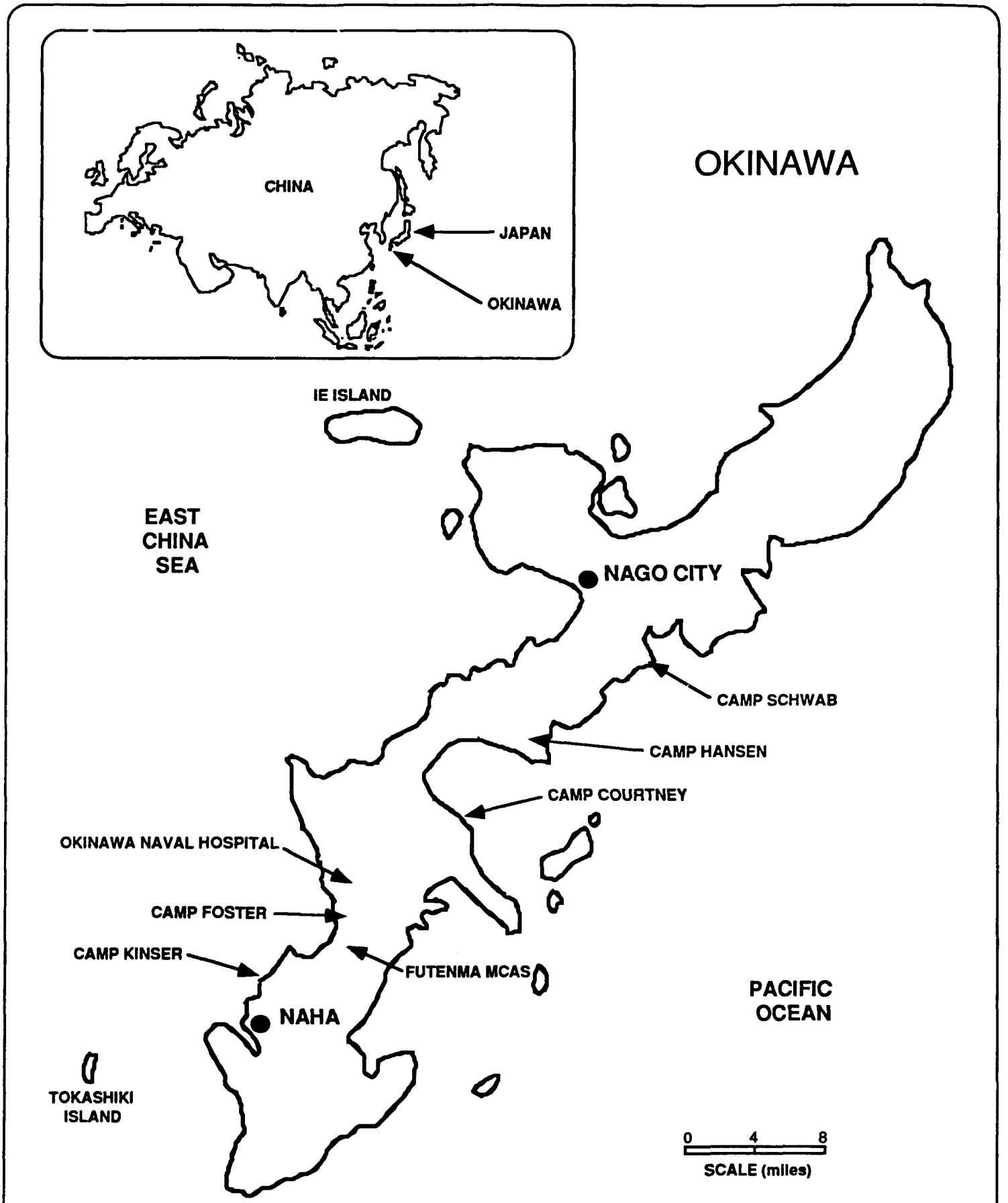

FIGURE 2. Map showing Okinawa study sites of the Viral Epidemiology Project.

Table A.
Additional Self-Reported Follow-Up Data Collected,
Prospective HTLV-I Seroconversion Study,
Active Duty Marine Corps Personnel*, Okinawa, Japan, 1989-1991

	Category	Number	Percent
Hepatitis/jaundice:	Yes	57	2.8
	No	2,012	97.2
	Not reported	3	-
Hepatitis type:	A	8	30.8
	B	10	38.5
	NonA/NonB	7	26.9
	C	1	3.8
	Not reported	34	-
	Not applicable	2,012	-
Hepatitis B vaccine:	Yes	128	6.5
	No	1,831	93.5
	Unknown/Not reported	113	-
Deployed:	Yes	881	42.6
	No	1,187	57.4
	Not reported	4	-
To Korea:	Yes	696	33.7
	No	1,371	66.3
	Not reported	5	-
To Philippines:	Yes	217	10.5
	No	1,850	89.5
	Not reported	5	-
To Thailand:	Yes	32	1.5
	No	2,035	98.2
	Not reported	5	-
To Other:	Yes	210	10.2
	No	1,857	89.8
	Not reported	5	-
Total:		**2,072**	

* Permanent personnel assigned to the 3rd MARDIV and 3rd FSSG MEF

Table A. continued
Additional Self-Reported Follow-Up Data Collected,
Prospective HTLV-I Seroconversion Study,
Active Duty Marine Corps Personnel*, Okinawa, Japan, 1989-1991

	Category	Number	Percent
Traveled:	Yes	604	29.4
	No	1,453	70.6
	Not reported	15	-
To Taiwan:	Yes	19	0.9
	No	2,037	99.1
	Not reported	16	-
To China:	Yes	23	1.1
	No	2,033	98.9
	Not reported	16	-
To Korea:	Yes	222	10.8
	No	1,834	89.2
	Not reported	16	-
To Philippines:	Yes	129	6.3
	No	1,927	93.7
	Not reported	16	-
To India:	Yes	6	0.3
	No	2,050	99.7
	Not reported	16	-
Hospitalized:	Yes	133	7.3
	No	1,678	92.7
	Not reported	261	-
Hospitalization type:	Blood related	1	0.8
	Other	131	99.2
	Not reported	262	-
	Not applicable	1,678	-
Tattoos applied:	Yes	108	6.0
	No	1,700	94.0
	Not reported	264	-
Tattoo location:	United States	5	5.2
	Thailand	3	3.1
	Philippines	21	21.6
	Okinawa	67	69.1
	Hong Kong	1	1.0
	Not reported	275	-
	Not applicable	1,700	-
Total:		2,072	

PUBLICATIONS and MEETING ABSTRACTS

PUBLICATIONS (to include related work):

1. Brodine SK, Oldfield EC, Blattner WA, et al: HTLV-I Among U.S. Marines Stationed in a Hyperendemic Area: Evidence for Female-to-Male Sexual Transmission. Journal of AIDS **1992**;5:158-162.

2. Brodine SK, et al.: HTLV-I and Hepatitis Viruses A, B, and C in U.S. Marines Stationed in Okinawa, Japan. In preparation **1992**.

3. Brodine SK, Thomas RJ: The Neuroepidemiology of HTLV-I. In: Molgaard CA (Ed.), Neuroepidemiology: Theory and Method, (109-128). Academic Press **1992**.

4. Molgaard CA and Brodine SK: Epidemiologic Concepts. Encyclopedia of Microbiology **1992**;2:5369-5373.

5. Lal RB, Brodine SK, Kazura J, Mbidde-Katonga E, Yanagihara R, and Roberts CR: Sensitivity and Specificity of a Recombinant Transmembrane Glycoprotein (rgp21)-Spiked Western Immunoblot for Serological Confirmation of Human T-Cell Lymphotropic Virus Type I and Type II Infections. Journal of Clinical Microbiology **1992**;30(2):296-299.

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7. Lal RB, Brodine SK, Coligan JE, and Roberts CR: Differential Antibody Responsiveness to p19 GAG Results in Serological Discrimination Between Human T Lymphotropic Virus Type-I and Type-II. Journal of Medical Virology **1991**;35:232-236.

8. Roberts CR, Mitra R, Hyams C, Brodine SK, and Lal RB: Serological Differentiation of HTLV-I from HTLV-II Infection by Synthetic Peptide Immunoassays. Accepted for publication Journal of Medical Virology **1992**.

PRESENTATIONS OF PAPERS AT INTERNATIONAL/NATIONAL CONFERENCES/MEETINGS:

1. Brodine SK: Survey of HTLV-I Seroprevalence in Marines Stationed on Okinawa. Epidemiology of Retroviruses. Walter Reed Army Institute of Research, Washington, DC. December, 1988

2. Brodine SK: Featured speaker on HTLV-I. Tri-Service Infectious Disease Meeting. Miami, Florida, 1990

3. Brodine SK: Featured speaker on Epidemiology of HTLV-I. Green College, Oxford University, Oxford, England, 1990

4. Brodine SK: HTLV Infections in Active Duty Personnel. San Diego Epidemiology Research Exchange. San Diego, California, May 1991.

5. Brodine SK: Panel member at the Workshop on the Epidemiology of Retroviral Infections - WRAIR. Cited in Wohlhieter, J: Epidemiology of Retroviral Infections - Military Medical Consortium for Applied Retroviral Research. Military Medicine **1992**;157:204-207.

ABSTRACTS:

1. Brodine SK, Oldfield EC, Corwin AL, et al: Seroprevalence of HTLV-I Among U. S. Marines Stationed in a Hyperendemic Area. (Abstract No. 0833) In Program and Abstracts of 5th International Conference on AIDS, Montreal, Canada. June 1989.

2. Brodine SK, Roberts CR, Holmberg J, et al: HTLV Infections in a Military Blood Donor Population. In Program and Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy, 1990.

3. Roberts C, Mitra R, Brodine S, Lal R: Serological Differentation of HTLV-I from HTLV-II Infection by Synthetic Peptide Immunoassay. 4th International HTLV Conference, 1991.

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BUDGET

FY 88 to 91 HTLV-I Seroconversion Study

FY 88 HTLV-I Seroconversion Study Funding Analysis

Authorization: $143,700.00
Document Number:

Description	JON	Authorization	Obligations	Expenditures
Training and Travel	X0641	$ 22,878.27	$ 22,878.27	$ 22,878.27
Supplies and Salaries	X0642	$ 31,677.92	$ 31,677.92	$ 31,677.92
Equipment	X0643	$ 12,598.00	$ 12,598.00	$ 12,598.00
Contracts	X0644	$ 72,800.00	$ 72,800.00	$ 72,800.00
Grand Total		$139,954.19	$139,954,19	$139,954.19

FY 89 HTLV-I Seroconversion Study Funding Analysis

Authorization: 166,000 + [3,745.81] = $169,745.81
Document Number: N0007589WR00030

Description	JON	Authorization	Obligations	Expenditures
Training and Travel	X0641	$ 14,042.43	$ 14,042.43	$ 14,042.43
Supplies and Salaries	X0642	$ 65,758.96	$ 63,642.00	$ 63,642.00
Equipment	X0643	$ 5,492.00	$ 5,492.00	$ 5,492.00
Contracts	X0644	$ 24,000.00	$ 24,000.00	$ 24,000.00
Grand Total		$109,293.39	$107,176.43	$107,176.43

FY 90 HTLV-I Seroconversion Study Funding Analysis

Authorization: 136,000 + [62,569.38] = $198,569.38
Document Number: N0007590WR00003

Description	JON	Authorization	Obligations	Expenditures
Training and Travel	X0641	$ 18,097.83	$ 18,097.83	$ 18,097.83
Okinawa Study Site Support		$ 69,000.00	$ 69,000.00	$ 51,742.40
Equipment	X0643	$ 4,725.45	$ 4,725.45	$ 4,725.45
Contracts	X0644	$ 1,464.00	$ 1,464.00	$ 1,464.00
Grand Total		$ 93,287.28	$ 93,287.28	$ 76,029.68

FY 91 HTLV-I Seroconversion Study Funding Analysis

Authorization: [$122,539.70]
Document Number: None

Description	JON	Authorization	Obligations	Expenditures
Training and Travel	X0641	$ 13,659.00	$ 13,659.00	$ 13,659.00
Okinawa Study Site Support		$ 45,000.00	$ 45,000.00	$ 45,000.00
Contracts	X0644	$ 35,000.00	$ 35,000.00	$ 35,000.00
Indirect Costs		$ 22,000.00	$ 22,000.00	$ 22,000.00
Labor		$ 5,600.00	$ 5,600.00	$ 5,600.00
Grand Total		$121,259.00	$121,259.00	$121,259.00

$1,280.70

QUESTIONNAIRES

INTAKE QUESTIONNAIRE
VIRAL EPIDEMIOLOGY PROJECT

DO NOT WRITE IN THIS COLUMN ADMINISTRATIVE USE ONLY

1. Name: _____ (Last Name First Name M.I.) _____ 1.

Duty Telephone: _____

2. Date this section completed: ____ ____ ____ M M D D Y Y 2.

3. Social Security Number: ____-____-_____ ____ ____ ____ 3.

____ ____

____ ____ ____

4. Current Pay Grade: (circle one)

1. E1	7. E7	13. 04	19. W3
2. E2	8. E8	14. 05	20. 20
3. E3	9. E9	15. 06	88. Other
4. E4	10. 01	16. 07-010	99. Unknown
5. E5	11. 02	17. W1	
6. E6	12. 03	18. W2	

____ 4.

5. Sex: (circle one)

1. Male
2. Female

____ 5.

6. Race: (circle one)

1. White (Non-Hispanic)
2. Black
3. Hispanic
4. Oriental (Chinese, Japanese)
5. Pacific Islander/Malayan (ex. Philipino)
6. American Indian
7. Vietnamese or other S.E. Asian
8. Other (Specify) _____

____ 6.

7. Date of Birth: ____ ____ ____ (Month Day Year) M M D D Y Y 7.

8. Place of Birth: _____ (City) ___ ___ ___ C C C 8.

_____ (State) ___ ___ S S

_____ (Country) ___ ___ C C

_____ 1.

9. Service Occupation:

1. Marine Corps MOS _____
2. Navy NEC _____

_____ 9.

10. Base (Camp) where you work: (circle one)

1.	Camp Courtney	6.	Camp Lester
2.	Camp Hansen	7.	Futenma
3.	Camp Schwab	8.	Camp Shields
4.	Camp Kinser	9.	Camp Foster/Butler
5.	Northern Training Area	88.	Other
		99.	Unknown

__ __ 10.

11. Base (Camp) where your medical records are maintained: (circle one)

1.	Camp Courtney	6.	Camp Lester
2.	Camp Hansen	7.	Futenma
3.	Camp Schwab	8.	Camp Shields
4.	Camp Kinser	9.	Camp Foster/Butler
5.	Northern Training Area	88.	Other
		99.	Unknown

__ __ 11.

12. Base (Camp) where you live: (circle one)

1.	Camp Courtney	7.	Camp Lester
2.	Camp Hansen	8.	Futenma
3.	Camp Schwab	9.	Camp Shields
4.	Camp Kinser	10.	Camp Foster/Butler
5.	Northern Training Area	11.	Kadena
6.	Plaza Housing	88.	Other

__ __ 12.

13. Your component of the Fleet Marine Force: (circle one)

1. Division
2. Group
3. Wing
8. Other

__ 13.

14. Unit assigned to on Okinawa:

1. Battalion _____
2. Company _____
3. Platoon _____
4. Squad _____

__ 14.

15. Date of arrival on Okinawa: _____/_____ (Month / Year) M M Y Y 15.

16. Projected rotation date: _____/_____ (Month / Year) M M Y Y 16.

17. Length of military service:

_____ year(s) and _____ month(s)

18. EAOS (End of Active Duty Obligated Service):

_____/_____
Month Year

19. Permanent home address:

_____
Number and Street

_____
City State ZIP

20. Permanent home phone number:

(_____) _____

21. Last duty station: _____

_____

22. Have you had any prior rotations on Okinawa? (circle one)

1. Yes
2. No

If yes to Question 22, list the prior rotations in items 23-26 below:

		Month Year		Month Year
23.	1.	_____/_____	-	_____/_____
24.	2.	_____/_____	-	_____/_____
25.	3.	_____/_____	-	_____/_____
26.	4.	_____/_____	-	_____/_____

_____ 1.

Y Y M M 17.

M M Y Y 18.

_ _ _ _ 19.

_ _ _ 20.

_ _ _ _ _ _

_ _ _ 21.

_ 22.

M Y M Y 23.

M Y M Y 24.

M Y M Y 25.

M Y M Y 26.

27. Current marital status: (circle one)

1. Single, never married
2. Married, living together on Okinawa
3. Married, temporarily separated while living on Okinawa
4. Divorced
5. Widowed
6. Legally Separated

28. Education: (circle highest level attained)

1. Did not graduate from high school
2. High school graduate or equivalent
3. Associate degree
4. Bachelor's degree
5. Master's degree
6. Doctorate degree

____ 1.

____ 27.

____ 28.

8/7/89

FOLLOW-UP QUESTIONNAIRE
'TIRAL EPIDEMIOLOGY PROJECT

1. Name: _____

2. Today's date: ____/__/____ (Month Day Year) _ _/_ _/_ _ 2.

3. Social Security Number: _____ _ _ _ 3.
_ _
_ _ _ _

4. Prospective Study ID #: _____ _ _ _ _ _ 4.

5. Year F/U: ____ _ _ 5.

6. Unit Address: _____
_____
_____

7. Projected rotation date: ____/____ (Month Year) _ _/_ _ 7.

8. Next duty station: _____ _ _ 8.
_____

9. Have you ever had Hepatitis or Yellow Jaundice? _ 9.

1. Yes
2. No

If yes, when: ____/____ (Month Year) _ _/_ _

If yes, what type of hepatitis: _
1. A
2. B
3. Non A/Non B
9. Unknown

10. Have you been immunized/vaccinated against hepatitis B? _ 10.

1. Yes
2. No

If yes, when (year) _____ _ _

11. Have you deployed from Okinawa during the past year? _ 11.

1. Yes
2. No

Please check the places you deployed to:

Korea (Bearhunt, Team Spirit) _____
How long (months)? _____ _ _

Philippines _____
How long (months)? _____ _ _

Thailand (Cobra Gold) _____
How long (months)? _____ _ _

Other (please state) _____ _ _
How long (months)? _____ _ _

12. Have you travelled from Okinawa to any other locations for leave or other reasons? _ 12.

1. Yes
2. No

Check the following that apply:

Taiwan _____	How long (months): _____	_ _
China _____	How long (months): _____	_ _
Korea _____	How long (months): _____	_ _
Phillipines ___	How long (months): _____	_ _
India _____	How long (months): _____	_ _

13. Have you had any sexually transmitted diseases (STDs) during the past year? (Syphilis, Gonorrhea, NGU) _ 13.

1. Yes
2. No

If yes, what type? (please circle) _
1. Syphilis
2. Gonorrhea
3. Chlamydia
4. Genital Warts
5. NGU
6. Other (specify) _____

Type of STD: _____ When? _____ Where? _____ _ _ _/_ _ _ _

Type of STD: _____ When? _____ Where? _____ _ _ _/_ _ _ _

14. Have you had symptoms of difficulty or burning with urination or discharge during the past year? _ 14.

1. Yes
2. No

If yes, Date: ____/____, Location: _____ _ _/_ _
Month Year _ _

Date: ____/____, Location: _____ _ _/_ _
Month Year _ _

Date: ____/____, Location: _____ _ _/_ _
Month Year _ _

15. Have you had sex with any Okinawans during this present tour? _ 15.

1. Yes
2. No

If yes, when: ____/____ _ _/_ _
Month Year

Number of sexual partners: _____ _ _

Estimated total number of times you had sex: ____ _ _ _

16. Have you been hospitalized during the past year? _ 16.

1. Yes
2. No

If yes, for what reason(s):

_____ _ _
Where? _____ _ _

17. Have you received any blood transfusions this past year? _ 17.

1. Yes
2. No

If yes, which hospital: _____ _ _

18. Have you worked with blood or blood products during this past year (i.e., dental, lab, clinical work)? _ 18.

1. Yes
2. No

19. Did you have any tattoos put on this past year? _ 19.

1. Yes
2. No

If yes,

Tattoo 1: _____ When: ____/____ __/__
(Location of tattoo parlor) Month Year

Tattoo 2: _____ When: ____/____ __/__
(Location of tattoo parlor) Month Year

Tattoo 3: _____ When: ____/____ __/__
(Location of tattoo parlor) Month Year

20. Have you ever had pneumonia? _ 20.

1. Yes
2. No

21. Have you had pneumonia during this past year? _ 21.

1. Yes
2. No

Viral Epidemiology Project Questionnaire
for RETIRED or ACTIVE DUTY Military Personnel

1. Study ID Number: R R _ _ _ _ _ _._

2. Specimen Number:

   1) _ _ _ _ _ _ 2) _ _ _ _ _ _ 3) _ _ _ _ _ _

3. Was this questionnaire completed by the nurse: 1 Yes 2 No

4. Interviewer: _ _ 5. Accessioning site: _ _

6. Referred by: _____ 7. Today's Date: _ _-_ _-_ _ (M M D D Y Y)

8. Gender: 1 Male 2 Female 9. SSN: _ _ _-_ _-_ _ _ _

10. Last Name: _____ First Name, MI: _____

11. Address: _____ _____ _____

12. Telephone # Home: _____ Work: _____

13. Ethnic Origin:

1 White (non-Hispanic)	2 African American (non-Hispanic)
3 Hispanic	4 Asian/SE Asian (not Japanese)
5 Okinawan	6 Japanese (not from Okinawa)
7 Native American	8 Pacific Islander/Malayan (Philippino)
9 Missing	0 Other _____

14. Highest level of education completed:

1 Did not complete HS	2 HS diploma or GED
3 Some college	4 Associate Degree
5 Bachelor's Degree	6 Master's or Above
	9 Missing

15. Age: _ _ 16. Date of birth: _ _-_ _-_ _ (M M D D Y Y)

17. City of Birth: _____ _ _ _ _

18. State of Birth: _____ _ _ (00 if not US)

19. Country of Birth: _____ _ _

20. Mother's Country of birth: _____ _ _

21. Father's Country of birth: _____ _ _

22. Military Service Affiliation: (if retired, check last service)

1 Navy 2 Marine Corp 9 Missing
3 Air Force 4 Army 5 Other _____

23. Retiree's Organization/Affiliation:

8 Not retired 0 None 9 Missing
1 MWR, Kinser 2 AAFES Taxi, Kadena 3 USMC retiree
4 VFW Amer Legion 5 Base Clubs System 6 Other _____

24. Total number of years served on active duty: __ __

25. Number of active duty years spent on Okinawa: __ __

26. Number of non-active duty years spent on Okinawa: __ __

27. Total number of years on Okinawa: __ __

28. If retired, what year did you retire from service: (if not retired enter 0 0) __ __ (Y Y)

29a. Have you ever received a blood transfusion: 1 Yes 2 No 9 Missing

29b. If yes, how many times: __ (if no, enter 0)

30. Have you had any major diseases: 1 Yes 2 No 9 Missing

31. If yes, what types: (if no, enter 0)

31a. _____ __

31b. _____ __

31c. _____ __

32. Do you have any Nervous System, Muscular, or Arthritic symptoms:

1 Yes 2 No 9 Missing

33. If yes, what types: 0 No Symptoms/NA 9 Missing
1 Spasticity 2 Stiffness 3 Urinary incontinence
4 Weakness 5 Numbness 6 Joint pain
7 Other _____

34a. Marital Status:

1 Single (never married) 2 Married
3 Divorced or Separated 4 Widowed 9 Missing

34b. If married, current spouse's Name: _____ _____

35. Age of Spouse: __ __ 00 Not Married 99 Missing

36. Current Spouse's Ethnic Origin:

1 White (non-Hispanic) 2 African American (non-Hispanic)
3 Hispanic 4 Asian/SE Asian (not Japanese)
5 Okinawan 6 Japanese (not from Okinawa)
7 Native American 8 Pacific Islander/Malayan (Philippino)
9 Missing 0 Other _____

37. Spouse's country of birth: _____ __ __

38. Date married: __ __ - __ __ - __ __
M M D D Y Y

39. Approximate year you began dating your spouse: __ __
Y Y

40. Total number of years in this relationship: __ __

41. Number of marriages, including this one: 0 Never married
1 2 3 4 5 6 7 8 9 Missing

42. If previously married, most recent prior spouse's Ethnic Origin:

1 White (non-Hispanic) 2 African American (non-Hispanic)
3 Hispanic 4 Asian/SE Asian (not Japanese)
5 Okinawan 6 Japanese (not from Okinawa)
7 Native American 8 Pacific Islander/Malayan (Philippino)
9 Missing 0 Other _____

Complete this section if spouse does not answer RSAS questionnaire or if widowed.

43. Does your spouse have any major diseases: 0 Not Married
1 Yes 2 No 9 Missing

44. If yes, what types: (if no, enter 0)

44a. _____ __

44b. _____ __

44c. _____ __

45a. Does your spouse have any family history of leukemia: 0 Not Married
1 Yes 2 No 9 Unknown

45b. If yes, give relationship: 0 if none 9 Missing
1 Father 2 Mother 3 Brother 4 Sister
5 Uncle/Aunt 6 Cousin 7 Grandparent 8 Other _____

46a. Does your spouse have any family history of cancer: 0 Not Married
1 Yes 2 No 9 Unknown

46b. If yes, give relationship: 0 if none 9 Missing
1 Father 2 Mother 3 Brother 4 Sister
5 Uncle/Aunt 6 Cousin 7 Grandparent 8 Other _____

47a. Spouse family history of nervous system disorders: 0 Not Married
1 Yes 2 No 9 Unknown

47b. If yes, give relationship: 0 if none 9 Missing
1 Father 2 Mother 3 Brother 4 Sister
5 Uncle/Aunt 6 Cousin 7 Grandparent 8 Other _____

47c. If yes, disease type: _____

48. How many children do you have from your current spouse:
8 Not married 9 Missing
0 None 1 2 3 4 5 6 7

49. Ages of children: (00 00 If not applicable)

49a. #1 __ __ __ __ (oldest child first in years and months)
49b. #2 __ __ __ __
49c. #3 __ __ __ __
49d. #4 __ __ __ __
49e. #5 __ __ __ __
49f. #6 __ __ __ __
49g. #7 __ __ __ __
Years Months

Viral Epidemiology Project Questionnaire
for SPOUSE of Retired or Active Duty Military Personnel

1. Study ID Number: R S _ _ _ _ _ _ _

2. Specimen Number:

   1) _ _ _ _ _ _ 2) _ _ _ _ _ _ 3) _ _ _ _ _ _

3. Was this questionnaire completed by the nurse: 1 Yes 2 No

4. Interviewer: _ _ 5. Accessioning site: _ _

6. Referred by: _____ 7. Today's Date: _ _-_ _-_ _ (M M D D Y Y)

8. Gender: 1 Male 2 Female 9. SSN: _ _ _-_ _-_ _ _ _

10. Last Name: _____ First Name, MI: _____

11. Address: _____ _____ _____

12. Telephone # Home: _____ Work: _____

13. Ethnic Origin:

1 White (non-Hispanic)	2 African American (non-Hispanic)
3 Hispanic	4 Asian/SE Asian (not Japanese)
5 Okinawan	6 Japanese (not from Okinawa)
7 Native American	8 Pacific Islander/Malayan (Philippino)
9 Missing	0 Other _____

14. Age: _ _ 15. Date of birth: _ _-_ _-_ _ (M M D D Y Y)

16. City of Birth: _____ _ _ _ _

17. State of Birth: _____ (00 if not US)

18. Country of Birth: _____ _ _

19. Mother's Country of birth: _____ _ _

20. Father's Country of birth: _____ _ _

21. Number of marriages, including current one:
    1 2 3 4 5 6 7 8 9 Missing

22. If previously married, most recent prior spouse's Ethnic Origin:

1 White (non-Hispanic)	2 African American (non-Hispanic)
3 Hispanic	4 Asian/SE Asian (not Japanese)
5 Okinawan	6 Japanese (not from Okinawa)
7 Native American	8 Pacific Islander/Malayan (Philippino)
9 Missing	0 Other _____

23a. Have you ever received a blood transfusion: 1 Yes 2 No 9 Missing

23b. If yes, how many times: __ (if no, enter 0)

24. Have you had any major diseases: 1 Yes 2 No 9 Missing

25. If yes, what types: (if no, enter 0)

25a. _____ __

25b. _____ __

25c. _____ __

26a. Do you have any Nervous System, Muscular, or Arthritic symptoms:
1 Yes 2 No 9 Missing

26b. If yes, what types:

0 No Symptoms/NA	9 Missing	
1 Spasticity	2 Stiffness	3 Urinary incontinence
4 Weakness	5 Numbness	6 Joint pain
7 Other _____		

27a. Do you have any family history of leukemia:
1 Yes 2 No 9 Unknown

27b. If yes, give relationship:

0 if none	9 Missing		
1 Father	2 Mother	3 Brother	4 Sister
5 Uncle/Aunt	6 Cousin	7 Grandparent	8 Other _____

28a. Do you have any family history of cancer:
1 Yes 2 No 9 Unknown

28b. It yes, give relationship:

0 if none	9 Missing		
1 Father	2 Mother	3 Brother	4 Sister
5 Uncle/Aunt	6 Cousin	7 Grandparent	8 Other _____

29. Do you have any family history of nervous system disorders:
1 Yes 2 No 9 Unknown

29b. If yes, give relationship: 0 if none 9 Missing
1 Father 2 Mother 3 Brother 4 Sister
5 Uncle/Aunt 6 Cousin 7 Grandparent 8 Other _____

29c. If yes, disease type: _____

30. How many children do you have from your current spouse:
8 Not married 9 Missing
0 None 1 2 3 4 5 6 7

31. Ages of children: (00 00 If not applicable)

31a. #1 __ __ __ __ (oldest child first in years and months)
31b. #2 __ __ __ __
31c. #3 __ __ __ __
31d. #4 __ __ __ __
31e. #5 __ __ __ __
31f. #6 __ __ __ __
31g. #7 __ __ __ __
Years Months

32. Were you breast fed as a child:
1 Yes 2 No 9 Unknown/Missing

33. Did you breast feed your children: 0 No children
1 Yes 2 No 9 Missing

34. If yes, approximately for how many months:

34a. #1 __ __ (00 If not applicable)
34b. #2 __ __
34c. #3 __ __
34d. #4 __ __
34e. #5 __ __
34f. #6 __ __
34g. #7 __ __
Months

Viral Epidemiology Project Data Management System
Blood Donors Questionnaire Cover Sheet

1. Interview Date: __ __/__ __/__ __ (M M D D Y Y) 2. IDNo: BD/__ __ __/__ __

3. SSN: __ __ __-__ __-__ __ __ __

4. Last Name: _____ First Name: _____

5. Address: _____ (Street)

_____ (City) _____ (State) _____-_____ (Zip code)

6a. Telephone: Home: (____) ____-_____ Work: (____) ____-_____

6b. Date last verified: __ __/__ __/__ __ (M M D D Y Y)

Viral Epidemiology Project Data Management System
Blood Donors Questionnaire

1. Interview Date: __ __/__ __/__ __ (M M D D Y Y) 2. IDNo: BD/__ __ __/__ __

3. SSN: __ __ __-__ __-__ __ __ __

7. Referral blood donor site: N/A

_____ Center _____ City ___ State _____ Country

8. Reason for referral:
   1 identified as HTLV positive
   2 spouse of HTLV blood donor
   3 child of HTLV blood donor

9. Service affiliation: (circle one)
   0 Not Applicable
   1 U.S. Navy 2 U.S. Marine Corps 3 U.S. Army
   4 U.S. Air Force 5 Other: _____

10. Status: (circle one)
   1 Active Duty 2 Retired
   3 Dependent 4 Other: _____

11. Current or Retired Pay Grade: (circle one)

1	E1	7	E7	13	O4	19	W3
2	E2	8	E8	14	O5		
3	E3	9	E9	15	O6	00	Not applicable
4	E4	10	O1	16	O7-O10		
5	E5	11	O2	17	W1		
6	E6	12	O3	18	W2		

12. Sex: 1 Male 2 Female

13. Race:
   1 White (Non-Hispanic)
   2 African American
   3 Hispanic
   4 Japanese (excluding Okinawan)
   5 Okinawan
   6 Pacific Islander/Malayan (ex: Philippino)
   7 Native American
   8 Vietnamese, Chinese, or other SE Asian
   0 Other (specify) _____ 9 Missing

IDNo: BD/__ __ __/__ __

14. Age: _____ 15. Date of birth: __ __/__ __/__ __
M M D D Y Y

16. Place of birth: _____ (City) _ _ _ _ _

_____ (State) _ _

_____ (Country) _ _

17. Unit assigned to:

_____ _ _ _

_____ _ _ _

_____ _ _ _

18a. Length of Military Service:
YY MM

18b. EAOS (End of Active Duty Obligated Service):

____/____ (enter 00/00 if not applicable)
MM YY

19. Current marital status:
1 Single, never married
2 Married
3 Divorced
4 Widowed
5 Legally Separated

20. Education: (circle highest level attained)
1 Did not graduate from high school
2 High school graduate or equivalent
3 Associate degree
4 Bachelor's degree
5 Master's degree
6 Doctorate degree

FAMILY HISTORY

21. Birthplace of your natural mother:

_____ City _ _ _ _

_____ State/Province _ _

_____ Country _ _

22. Birthplace of your natural father:

_____ City _ _ _ _

_____ State/Province _ _

_____ Country _ _

IDNo: BD/__ __ __/__ __

23. What is the race of your mother:
1 White (Non-Hispanic)
2 African American
3 Hispanic
4 Japanese (excluding Okinawan)
5 Okinawan
6 Pacific Islander/Malayan (ex: Philippino)
7 Native American
8 Vietnamese, Chinese, or other SE Asian
0 Other (specify) _____ 9 Missing

24. What is the race of your father:
1 White (Non-Hispanic)
2 African American
3 Hispanic
4 Japanese (excluding Okinawan)
5 Okinawan
6 Pacific Islander/Malayan (ex: Philippino)
7 Native American
8 Vietnamese, Chinese, or other SE Asian
0 Other (specify) _____ 9 Missing

25. Birthplace of your spouse/previous spouse:
A. Spouse: (enter 0 if N/A)

_____ City _ _ _ _

_____ State/Province _ _

_____ Country _ _

B. Previous Spouse: (enter 0 if N/A)

_____ City _ _ _ _

_____ State/Province _ _

_____ Country _ _

26. A. When you began dating spouse: (enter 00/00 if N/A) ____/____ MM YY

Date you married spouse: (enter 00/00 if N/A) ____/____ MM YY

B. When you began dating previous spouse: (enter 00/00 if N/A) ____/____ MM YY

Date you married previous spouse: (enter 00/00 if N/A) ____/____ MM YY

27. What is the race of your spouse:

A. Current Spouse:

1 White (Non-Hispanic)
2 African American
3 Hispanic
4 Japanese (excluding Okinawan)
5 Okinawan
6 Pacific Islander/Malayan (ex: Philippino)
7 Native American
8 Vietnamese, Chinese, or other SE Asian
0 Other (specify) _____ 9 Missing

B. Previous Spouse:

1 White (Non-Hispanic)
2 African American
3 Hispanic
4 Japanese (excluding Okinawan)
5 Okinawan
6 Pacific Islander/Malayan (ex: Philippino)
7 Native American
8 Vietnamese, Chinese, or other SE Asian
0 Other (specify) _____ 9 Missing

28. Have you had any major diseases:

1 Yes 2 No 9 Missing

If yes, what types (coding after)

28a. _____ (0 if N/A) __
28b. _____ (0 if N/A) __
28c. _____ (0 if N/A) __

29. Do you have any Nervous System, Muscular, or Arthritic symptoms:

1 Yes 2 No 9 Missing

29a. If yes, what types: 0 No Symptoms/NA

1 Spasticity 2 Stiffness 3 Urinary incontinence
4 Weakness 5 Numbness 6 Joint pain
7 Other _____ 9 Missing

30. Abnormal white blood cells:

1 Yes 2 No 9 Missing

A. What was the problem: _____

_____

B. When was this: ____/____ (00/00 if no)
MM YY

IDNo: BD/__ __ __/__ __

31. Have you ever had cancer:
1 Yes 2 No if yes:

A. What type of cancer: _____

B. Where in the body: _____

C. When did you have it: ____/____ (00/00 if no)
MM YY

32. Have you ever had a blood transfusion or a transfusion of red or white blood cells, platelets, or plasma:

1 Yes 2 No If yes:

A. How many transfusions: _____ (0 if no)

#1 B. What year was the most recent year of transfusion: ____
YY

C. Units received that year (most recent): _____

D. Where did you receive that transfusion:

_____ State _ _

_____ Country _ _

If more than one transfusion:

(enter 00 if N/A)
#2 E. What year was the transfusion before that: ____
YY

F. How many units: _____

G. Where did you receive that transfusion:

_____ State _ _

_____ Country _ _

(enter 00 if N/A)
#3 H. What year was the transfusion before that: ____
YY

I. How many units: _____

J. Where did you receive that transfusion:

_____ State _ _

_____ Country _ _

33. Have you given blood in the past 5 years:
1 Yes 2 No

If yes, list approximate date and location.
Start from the present and work backwards.

A. ____/____ (00/00 if no)
MM YY

_____ Base or Site _ _

_____ City _ _ _ _

_____ State _ _

_____ Country _ _

B. ____/____ (00/00 if no)
MM YY

_____ Base or Site _ _

_____ City _ _ _ _

_____ State _ _

_____ Country _ _

34. Have you ever had a sexually transmitted disease:
1 Yes 2 No 9 Missing

If yes, what types, where and when: (0 if no)

_____	_____	_____
_____	_____	_____
_____	_____	_____
STD type	Where	Date

35. Have you ever had sexual relations with anyone from the following:

35a.	IV drug abuser	1	Yes	2 No
35b.	Persons from Okinawa	1	Yes	2 No
35c.	Persons from southern Japan	1	Yes	2 No
35d.	Persons from Caribbean	1	Yes	2 No
35e.	Persons from South America	1	Yes	2 No
35f.	Persons from Central America	1	Yes	2 No

35g. Comments: _____

_____

_____

36. How many children do you have:

0 None 1 2 3 4 5 6 7 9 Missing

Ages of children: (0 0.0 0 If not applicable)

36a. #1 __ __.__ __ (oldest child first in years)
36b. #2 __ __.__ __ (use months if child < 1 year old)
36c. #3 __ __.__ __
36d. #4 __ __.__ __
36e. #5 __ __.__ __
36f. #6 __ __.__ __
36g. #7 __ __.__ __
Years Months

37. Were you breast fed as a child:
1 Yes 2 No 9 Unknown/Missing

Women Only:

38. Did you breast feed your children:
1 Yes 2 No 0 No children 9 Missing

If yes, approximately for how many months: (00 If not applicable)

38a. #1 __ __
38b. #2 __ __
38c. #3 __ __
38d. #4 __ __
38e. #5 __ __
38f. #6 __ __
38g. #7 __ __
Months